

~~---29(New). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit proliferation of cancer cells.~~

~~---30(New). The composition of claim 29, wherein said cancer cells are carcinoma cells.~~

SUB D6  
---31(New). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit a viral activity.

SUB F3  
C1  
SUB D7  
---32(New). The composition of claim 31, wherein said viral activity is viral-induced hemolysis.

---33(New). A composition comprising an acceptable carrier and a peptide according to claim 1 in an amount effective to inhibit growth of a protozoan.

---34(New). A mixture consisting of two or more non-hemolytic cytolytic peptides selected from the group consisting of a peptide according to claim 1, a peptide comprising one or both of L-amino acid residues and D-amino acid residues and an  $\alpha$ -helix breaker moiety, and a cyclic derivative thereof.

CHIEF  
---35(New). The mixture of claim 34, wherein each peptide present in the mixture consists of 12 amino acids, each of which is selected from the group consisting of L-Leu, D-Leu, L-Lys, and D-Lys.

c<sup>1</sup> --36(New). The complex according to claim 16 which is composed of five molecules of the same peptide or of different peptides.

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Please replace claims 1, 6-8, 10, 14-17, and 19-20 with new amended claims 1, 6-8, 10, 14-17, and 19-20 as follows below. A marked up version of the amended claims to show the changes made is attached hereto.

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D<sup>1</sup> 1(Amended). A non-hemolytic cytolytic peptide having a selective cytolytic activity manifested in that it has a cytolytic activity on pathogenic cells, said pathogenic cells being cells which are non-naturally occurring within the body consisting of microbial pathogenic organisms and malignant cells; and it is non-hemolytic, namely it has no cytolytic effect on red blood cells or has a cytolytic effect on red blood cells at concentrations which are substantially higher than that in which it manifests said cytolytic activity, said non-hemolytic cytolytic peptide being selected from the group consisting of:

- c<sup>2</sup>
- (A) a cyclic derivative of a peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising one or both of L-amino acid residues and D-amino acid residues, and comprising an  $\alpha$ -helix breaker moiety;

- C2
- (B) a peptide comprising both L-amino acid residues and D-amino acid residues, having a net positive charge which is greater than +1, and having a sequence of amino acids such that a corresponding amino acid sequence comprising only L-amino acid residues is not found in nature, and cyclic derivatives thereof;
- (C) a complex consisting of a plurality of 2 or more non-hemolytic cytolytic peptides, each peptide having a net positive charge which is greater than +1, and comprising both L-amino acid residues and D-amino acid residues, or comprising one or both of L-amino acid residues and D-amino acid residues and comprising an  $\alpha$ -helix breaker moiety, or cyclic derivatives of the foregoing, said peptides being linked together by the use of a linker molecule covalently bound to each of the peptides; and
- (D) a random copolymer consisting of a ratio of a hydrophobic, a positively charged and a D-amino acid.
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AB3  
C3

6 (Twice-amended). The cyclic peptide according to claim 1 selected from the cyclic pardaxin-derived peptides herein designated peptides **86-88** (SEQ ID NOs: 86-88, respectively), of the sequence:

86. Cyclic K<sup>1</sup>[D]P<sup>7</sup> L<sup>18</sup>L<sup>19</sup> [1-22]-par of the sequence:

Cys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-  
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys

87. Cyclic K<sup>1</sup> K<sup>2</sup>[D]P<sup>7</sup> L<sup>18</sup>L<sup>19</sup> [1-22]-par of the sequence:

Cys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-Ser-  
Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys

88. Cyclic K<sup>1</sup> K<sup>2</sup>K<sup>3</sup> [D]P<sup>7</sup> L<sup>18</sup>L<sup>19</sup> [1-22]-par of the sequence:

Cys-Lys-Lys-Lys-Gly-Phe-Phe-Ala-Leu-Ile-Pro-Lys-Ile-Ile-  
Ser-Ser-Pro-Leu-Phe-Lys-Thr-Leu-Leu-Ser-Ala-Val-Cys

C3  
7(Amended). The peptide according to claim 1 (B), comprising both L-amino acid residues and D-amino acid residues and having a sequence of amino acids such that a corresponding amino acid sequence comprising only L-amino acid residues is not found in nature.

SUB D<sup>2</sup>  
8(Amended). The peptide according to claim 7, having the following characteristics:

(a) it is a non-natural synthetic peptide composed of a ratio of at least one hydrophobic amino acid and at least one positively charged amino acid, and in which sequence at least one of the amino acid residues is a D-amino acid;

C3 (b) the peptide has a net positive charge which is greater than +1; and

(c) the ratio of hydrophobic to positively charged amino acids is such that the peptide is cytolytic to pathogenic cells but does not cause cytolysis of red blood cells.

sub g.1  
C4 10(Amended). The peptide according to claim 9, wherein the net positive charge greater than +1 is due to the amino acid composition or to the addition of positively charged chemical groups, or which hydrophobicity is decreased by the addition of polar amino acids selected from the group consisting of serine, threonine, methionine, asparagine, glutamine and cysteine.

WO 97/01007  
C5 14(Thrice-Amended). The cyclic derivative of a non-natural synthetic peptide according to claim 7, selected from the peptides herein designated 92-95 (SEQ ID NOs: 92-95, respectively), of the sequence:

92. Cyclic Cys Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys Cys

93. Cyclic Cys Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Lys Cys

94. HN - Lys Leu Leu Leu Lys Leu Leu Leu Lys Leu Leu Lys - CO

95. HN - Lys Leu Leu Leu Lys Leu Lys Leu Lys Leu Leu Lys - CO

15(Twice-Amended). A complex of peptides according to claim 1(C) consisting of a plurality of 2 or more non-hemolytic cytolytic peptides according to claim 1, said peptides being linked together through a linker molecule covalently bound to each of the peptides.

CS SUB D3 16(Amended). The complex according to claim 15, which is composed of 2 or more, molecules of the same peptide or of different peptides, and the linker is a peptide or a commonly used linker.

SUB 91 17(Twice-Amended). The complex according to claim 1, wherein the linked Lys/Leu diastereomers herein designated 96 and 97 are covalently linked together through a linker molecule:

96. ([D]-L<sup>3,4,8,10</sup>-K<sub>4</sub>L<sub>8</sub>C)<sub>5</sub> [D]-L<sup>3,4,8,10</sup>-K<sub>4</sub>L<sub>8</sub> of the sequence:

(Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-Cys-NH<sub>2</sub>)<sub>5</sub> Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH<sub>2</sub> (SEQ ID NOS: 96 and 23)

97. ([D]-L<sup>3,4,8,10</sup>-K<sub>5</sub>L<sub>7</sub>C)<sub>5</sub> [D]-L<sup>3,4,8,10</sup>-K<sub>4</sub>L<sub>9</sub> of the sequence:

(Lys-Leu-Leu-Leu-Lys-Leu-Lys-Leu-Lys-Leu-Leu-Lys-Cys-NH<sub>2</sub>)<sub>5</sub> Lys-Leu-Leu-Leu-Lys-Leu-Leu-Leu-Lys-Leu-Leu-Lys-NH<sub>2</sub> (SEQ ID NOS: 97 and 24).

Sub  
NE 91/

→ 19 (Amended). The mixture according to claim 36,  
comprising a mixture of Lys/Leu 12-mer peptide diastereomers.

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CP SOB  
D4

→ 20 (Amended). The non-hemolytic cytolytic random  
copolymer according to claim 1(D), consisting of different ratios  
of a hydrophobic, a positively charged and a D-amino acid.

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